--5. (amended) The method of claim 1, wherein after treatment the subject's HIV-1 viral load is reduced to 33% or less of the subject's HIV-1 viral load prior to administering the antibody to the subject.--

--6. (amended) The method of claim 1, wherein after treatment the subject's HIV-1 viral load is reduced to 10% or less of the subject's HIV-1 viral load prior to administering the antibody to the subject.--

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--7. (amended) The method of claim 1, wherein after treatment the reduction of the subject's HIV-1 viral load is sustained for a period of time.--

REMARKS

Claims 1-22 are pending in the application. Claims 1, and 5-7 have been amended, which amendments are completely supported by the application as originally filed. Thus the subject amendments do not raise any issue of new matter. Entry of this Amendment is therefore respectfully requested such that claims 1-22, as amended, will be pending in the application.

In the Office Action the Examiner states that this application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 C.F.R. §1.821 (a)(1) and (a)(2). The Examiner further states, however, that the application fails to comply with the requirements of 37 C.F.R. §§ 1.821-1.825 for the reason(s) set forth on the attached Notice to Comply With Requirements For Patent Applications Containing Nucleotide Sequence and/or Amino Acid Sequence Disclosures. The Examiner additionally states that failure to comply with these requirements in response to this Office Action will be considered to be [a] non-response and may

result in abandonment of this application. The Examiner also states that a reply to this notice to comply with the sequence rules should NOT be sent to the 20231 zip code address for the United States Patent and Trademark Office.

In response, Applicants submit that as noted above they have filed, under separate cover on the same day as the present Amendment, a "Response In Compliance With The Requirements For Patent Applications Containing Nucleotide Sequences and/or Amino Acid Sequences Set Forth in the Notice To Comply Attached to the June 25, 2002 Office Action" addressed to: Assistant Commissioner for Patents, U.S. Patent and Trademark Office, P.O. Box 2327, Arlington, VA 22202, Attn: Box Sequence. The subject Response is believed to address all of the issues raised in the Notice to Comply and thus to place the application in compliance with all of the requirements of 37 C.F.R. §§ 1.821 - 1.825.

The Examiner additionally states in the Office Action that claims 5-10 are rejected under 35 U.S.C. §112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicants regard as the invention. The Examiner goes on to state that claims 5-10 are vague and indefinite. He inquires whether the method requires that the viral load be reduced prior to treatment with the antibodies or whether the reduction is relative to the viral load prior to treatment. The Examiner thus recommends that the claims be amended to insert, after "wherein", the phrase --after treatment--.

In response to the above rejection under §112, second paragraph, Applicants have amended claims 5, 6, and 7 as suggested by the Examiner to insert the phrase --after treatment-- after "wherein" in the first line of each of the subject claims, thus clarifying

that the reduction recited in the claim is relative to the viral load prior to treatment. Claims 8-10 require no amendment due to their dependence on (amended) claim 7. The amendments to claims 5-7 are supported by the application as filed and thus do not add any new matter. They are believed to overcome the ground for rejection of claims 5-10 under §112 and the Examiner is therefore respectfully requested to reconsider and withdraw the §112 rejection of claims 5-10.

The Examiner states in the Office Action that claims 1-10, 21 and 22 are rejected under 35 U.S.C. §102 (a) as being anticipated by Olson et al. WO 00/35409. The Examiner further states that Olson et al. teach inhibiting the fusion of HIV-1 with CD4+CCR5+ cells by treating the cells with anti-CCR5 antibodies. The Examiner states that the reference specifically recites the same monoclonal antibodies as are claimed in the instant invention, namely, PA8, PA9, PA10, PA11, PA12 and PA14. The Examiner states that the amount of viral load reduction would be expected to be the same because it is a property of the specific antibodies that are administered. The Examiner states that Olson et al. teach on pages 13 and 20 that the antibody can be humanized. The Examiner states that it is disclosed on page 19 that the antibodies can be administered by intravenous, intramuscular or subcutaneous means. The Examiner states that, therefore, the instant invention is anticipated by Olson et al. Applicants respectfully traverse the rejection of claims 1-10, 21 and 22 under §102(a) for the reasons below.

The statute upon which the rejection is based, i.e., 35 U.S.C. §102 (a), reads as follows:

A person shall be entitled to a patent unless --

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

Thus, in order to sustain a rejection of claims 1-10, 21 and 22 under the subject statutory section, one or both of the following must be true:

(1) the invention recited in the rejected claims must have been known or used by *others* in this country *before* the invention thereof by the applicant for a patent; and/or

(2) the invention recited in the rejected claims must have been patented or described in a printed publication in this or a foreign country , *before* the invention thereof by the applicant for a patent.

With regard to item no. 1 above, Applicants note the definition of "by others" provided in the Manual of Patent Examining Procedure ("M.P.E.P.") §2132 (III). That is, according to the M.P.E.P., "[t]he term 'others' in 35 U.S.C. 102(a) refers to any entity which is different from the inventive entity. The entity need only differ by one person to be 'by others'. This holds true for all types of references eligible as prior art under 35 U.S.C. 102(a) including publications as well as public knowledge and use."

With the above definition in mind, Applicants respectfully direct the Examiner's attention to the fact that the named authors (i.e., inventors) of the Olson et al. WO 00/35409 reference are (1) William C. Olson and (2) Paul J. Maddon. Further, the inventors of the presently claimed invention *also* are, as recited on the Official Filing Receipt issued by the Patent Office, (1)

William C. Olson and (2) Paul J. Maddon. Thus, the invention clearly was **NOT** known or used by **OTHERS** (as that term is defined in the M.P.E.P.) before the invention thereof by the present applicants. The invention also was **NOT** patented or described in a printed publication in this or a foreign country **before the invention thereof** by the present applicants. That is, the present applicants **must** have invented the invention **prior to** describing it in the cited publication.

Therefore, as demonstrated above, the reference cited to reject claims 1-10, 21 and 22 under §102(a) does **not** meet **either** of the requirements of 35 U.S.C. §102(a) necessary to sustain a rejection under that section and thus the disclosure of applicants' own work in Olson et al. should not serve to bar allowance of the claims of the present application. The Examiner is thus respectfully requested to reconsider and withdraw the rejection of claims 1-10, 21 and 22 under §102 (a) based upon the comments provided above.

The Examiner additionally states in the Office Action that claims 1, 2 and 5-10 are rejected under 35 U.S.C. §102(b) as being anticipated by Vila-Coro et al., i.e., "HIV-1 infection through the CCR5 receptor is blocked by receptor dimerization", PNAS, March 28, 2000, vol. 97, no. 7, pp. 3388-3393. The Examiner states that Vila-Coro et al. teach that the administration of the disclosed antibody reduces HIV-1 (represented by RNA copy number) 10 fold for at least two weeks compared to animals treated with a control antibody, and therefore, the invention is anticipated by Vila-Coro et al. The §102(b) rejection based on Vila-Coro et al. is respectfully traversed for the reasons set forth below.

In order for a prior art reference to anticipate an invention, the reference must disclose every element of the invention. In the present application, claim 1 is the only independent claim. Claim 1 has been amended (see above) such that it now recites a method of reducing an HIV-1 infected subject's HIV-1 viral load which comprises administering to the subject *solely post-infection* an effective viral load reducing amount of an antibody which (a) binds to a CCR5 chemokine receptor and which (b) inhibits fusion of HIV-1 to a CD4+CCR5+ cell, so as to thereby reduce the subject's HIV-1 viral load to 50% or less of the subject's HIV-1 viral load prior to *any administration of* the antibody to the subject. In the invention as now recited in (amended) claim 1, therefore, the antibody is administered *only* to subjects who are already infected with HIV, i.e., solely post-infection.

In contrast to the invention as now claimed, however, the Vila-Coro reference cited to reject claims 1, 2 and 5-10 discloses a significantly different process. In the process disclosed by the reference, *uninfected* (i.e., with HIV) animals were initially pre-treated with a prophylactic dose of the CCR5-receptor specific mAB. These *pre-treated* animals were *only* exposed to the HIV virus *after* such antibody treatment, following which they were *again* treated, i.e., for a *second time* with the antibody in an effort to reduce their viral load. While, as noted in the Office Action, the HIV-1 viral load of such animals was reduced, there is no teaching provided by the authors as to how to determine whether this reduction is due (A) to the pre-treatment of the *uninfected animals* with the antibody, (B) to the subsequent treatment of the infected animals with the antibody, or (C) to some combination of these two treatment regimens. In contrast, claim 1 of the present application now specifically

recites that the subject antibody is administered to subjects **solely post-infection** (i.e., with HIV), thus **excluding** the treatment of uninfected subjects, as practiced by Vila-Coro, et al., with the subject antibody.

Moreover, further to the above, as described in Poignard, et al., "Neutralizing Antibodies Have Limited Effects on the Control of Established HIV-1 Infection In Vivo", Immunity, Vol. 10: 431-438 (April, 1999) and Gauduin, et al., "Passive Immunization With a Human Monoclonal Antibody Protects hu-PBL-SCID Mice Against Challenge by Primary Isolates of HIV-1", Nature Medicine, vol. 3, no. 12: 1389-1393 (December, 1997), **other** types of antibodies (e.g., IgG1b12 or "b12") that are sometimes effective in the pretreatment setting described by Vila-Coro, et al. **cannot** be predicted to be effective in treating **post-infection** subjects, which subjects are the focus of the present invention. Copies of the above-cited references are submitted herewith.

For the reasons above, applicants submit that the invention as recited in claim 1 is not anticipated by Vila-Coro et al. since the subject reference does not teach every element of the claimed invention. That is, the recitation in claim 1 to administer the antibody to subjects solely post-infection so as to thereby reduce the subject's viral load to 50% or less of the viral load prior to any administration of the antibody clearly differentiates the invention from the subject reference which requires the treatment of subjects prior to their infection with the human immunodeficiency virus (HIV). Claims 2 and 5-10, which depend directly or indirectly upon claim 1, are believed to be distinguishable over the cited reference for the same reasons as claim 1. The Examiner is therefore respectfully requested to reconsider and withdraw the rejection of claims 1, 2 and 5-10

under §102(b).

Claims 1-22 are rejected under 35 U.S.C. §103(a) as obvious over Olson et al. WO 00/35409. The Examiner states in the Office Action that the relevance of the reference is as discussed with regard to the §102(a) rejection thereover. The Examiner further states that the reference does not specifically teach the claimed dosages or schedule of administration. The Examiner states that it would have been obvious to one of ordinary skill in the art at the time the invention was made to vary the treatment regime to optimize the individual patient's response to the treatment. The Examiner states that the claimed dosages fall within the disclosed range of dosages at page 19 as well as the time intervals of multiple doses which, 'can be determined without undue experimentation by one skilled in the art' and therefore, that the instant invention is obvious over Olson et al. (WO 00/35409). Applicants respectfully traverse the subject rejection of claims 1-22 for the reasons set forth below.

In response to this rejection, applicants submit that they have established above, in the discussion of the § 102(a) rejection based on this reference, that the authors of the subject PCT publication (WO 00/35409) and the named inventors of the present application are identical, i.e., William C. Olson and Paul J. Maddon. Thus, both the reference and the present application name the same inventive entity. Clearly, therefore, the disclosure contained in WO 00/35409 is a disclosure of the applicants' own invention.

Section 715.01(c) of the Manual of Patent Examining Procedure (M.P.E.P.) discloses how to handle rejections based upon such disclosures. The relevant portion of the M.P.E.P. section states that, "Unless it is a statutory bar, a rejection based upon a

publication may be overcome by a showing that it was published either by applicant himself/herself or on his/her behalf." The published PCT application of Olson et al. is not a statutory bar to the presently claimed invention as established above in the discussion of the §102(a) rejection based on that reference. Furthermore, it is obvious that the PCT publication was published "on applicants' behalf." Thus, as noted above, the reference is simply an earlier publication of applicants' own invention. As such, the §103(a) rejection based on the reference is overcome due to the showing that the inventive entities cited in both the publication and the present application are identical. The Examiner is therefore respectfully requested to reconsider and withdraw the rejection of claims 1-22 under 35 U.S.C. §103(a) over WO 00/35409.

Claims 1-22 are additionally rejected under 35 U.S.C. §103(a) as obvious over the Vila-Coro et al. reference noted above. The Examiner states in the Office Action that the relevance of the reference is set forth in the discussion of the §102(b) rejection based upon that reference. The Examiner additionally states, however, that the reference does not specifically teach the claimed dosages or schedule of administration. The Examiner states that it would have been obvious to one of ordinary skill in the art at the time the invention was made to vary the treatment regime to optimize the individual patient's response to the treatment. The Examiner additionally states that the claimed dosages as well as the time intervals of multiple doses can not be determined without undue experimentation by one skilled in the art, and therefore that the instant invention is obvious over Vila-Coro et al. Applicants respectfully traverse the rejection of claims 1-22 over the subject reference for the reasons provided below.

As pointed out above in the discussion of the §102 rejection based on the Vila-Coro et al. reference, claim 1 (i.e., the only independent claim of this application) has been amended to recite that the invention is directed to a method (of reducing an HIV infected subject's HIV-1 viral load) which entails administering the antibody to the subject *solely post-infection.* In contrast, as also discussed above, Vila-Coro et al. teaches administering the antibody in two separate "rounds" or stages. The **first stage** involves a prophylactic administration provided to **uninfected** animals, after which the **antibody-treated** animals are exposed to the HIV virus. This exposure is thereafter followed by a **second round of antibody treatment** of the infected animals in an effort to reduce the viral load in the treated animals. The subject reference contains no teaching or disclosure which would suggest to one of ordinary skill in this art to dispense with the first round of treatments, i.e., treating the **uninfected** animals, and thus it fails to render obvious applicants' presently claimed invention which requires administration of the antibody **solely** to **infected** subjects. The Examiner is therefore respectfully requested to reconsider and withdraw the rejection of claims 1-22 under §103(a) over Vila-Coro et al.

Supplemental Information Disclosure Statement

In compliance with their duty of disclosure under 37 C.F.R. §1.56, applicants direct the Examiner's attention to the following above-discussed references, which are listed on a form PTO-1449 attached hereto as **Exhibit B**. Copies of these references are submitted as Attachments 1 and 2 to Exhibit B.

Poignard, et al., Neutralizing Antibodies Have Limited Effects on the Control of Established HIV-1 Infection

In Vivo, Immunity, vol. 10, 431-438 (April 1999) (Attachment 1).

Gauduin, et al., Passive Immunization With a Human Monoclonal Antibody Protects hu-PBL-SCID Mice Against Challenge By Primary Isolates of HIV-1, Nature Medicine, Vol. 3, No. 12, 1389-1393 (December 1997) (Attachment 2).

The Examiner is respectfully requested to make these references of record in the present application by initialing and dating the attached form PTO-1449 and returning a copy thereof to applicants' attorneys for their file. Applicants maintain that the subject references neither disclose nor suggest the invention claimed in the present application, whether viewed alone or in combination with any other cited reference(s).

A fee of One hundred eighty dollars ($180.00) is believed to be due for the submission of this Information Disclosure Statement. A check including this amount is enclosed herewith.

Summary

For all of the reasons set forth above, applicants respectfully submit that the amendments to the claims of the application and the remarks provided herein are believed to overcome all of the grounds for rejection of the claims. Reconsideration and withdrawal of these rejections is therefore respectfully solicited so that claims 1-22 may proceed to issuance.

If a telephone interview would be of assistance in advancing prosecution of the subject application, applicants' undersigned attorneys invite the Examine to telephone either of them at the number provided below.

A fee of Four Hundred Sixty Dollars ($460.00) is believed to be due for a three month extension of the time for filing (1) this Amendment, and (2) the Response in Compliance With The Requirements For Patent Applications Containing Nucleotide Sequences And/Or Amino Acid Sequences Set Forth In The June 25, 2002 Office Action, which is being filed under separate cover on the same day as the Amendment. In addition, as noted above, a fee of $180.00 is believed to be due with the Supplemental Information Disclosure Statement submitted herewith. Therefore, a check for $640.00 (i.e., $460.00 + $180.00) is included herewith. If any additional fees are required, authorization is hereby given to charge the amount of such fee(s) to Deposit Account No. 03-3125.

Respectfully submitted,

Mohca Farley

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I hereby certify that this correspondence is being deposited this date with the U.S. Postal Service with sufficient postage as first class mail in an envelope addressed to: Assistant Commissioner for Patents, Washington, D.C. 20231.

Mohca Farley 12-26-02

John P. White Date
Reg. No. 28,678
Mark A. Farley
Reg. No. 33,170

Exhibit A

--1. (amended) A method of reducing an [HIV] HIV-1 infected subject's HIV-1 viral load which comprises administering to the subject solely post-infection an effective viral load reducing amount of an antibody which (a) binds to a CCR5 chemokine receptor and (b) inhibits fusion of HIV-1 to a CD4+CCR5+ cell, so as to thereby reduce the subject's HIV-1 viral load to 50% or less of the subject's HIV-1 viral load prior to [administering] any administration of the antibody to the subject.--

--5. (amended) The method of claim 1, wherein after treatment the subject's HIV-1 viral load is reduced to 33% or less of the subject's HIV-1 viral load prior to administering the antibody to the subject.--

--6. (amended) The method of claim 1, wherein after treatment the subject's HIV-1 viral load is reduced to 10% or less of the subject's HIV-1 viral load prior to administering the antibody to the subject.--

--7. (amended) The method of claim 1, wherein after treatment the reduction of the subject's HIV-1 viral load is sustained for a period of time.--